

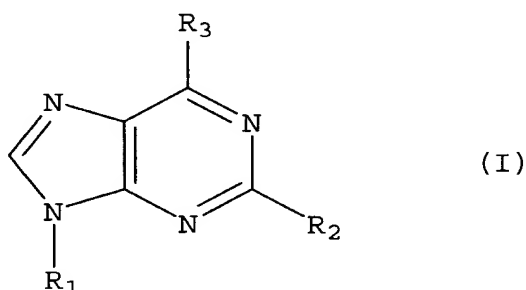
Amendments to the Claims

This listing of the claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

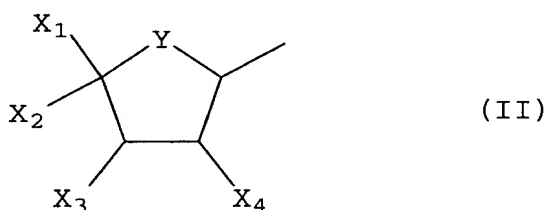
1 (Canceled)

2 (Currently Amended). The method of Claim ±39, wherein said A3RAg is a compound of the general formula (I):



wherein,

$R_1$  represents an alkyl, hydroxyalkyl, carboxyalkyl or cyanoalkyl or a group of the following general formula (II):



in which:

- Y represents an oxygen or sulfur atom or  $CH_2$ ;
- $X_1$  represents H, alkyl,  $R^aR^bNC(=O)-$  or  $HOR^c-$ ,

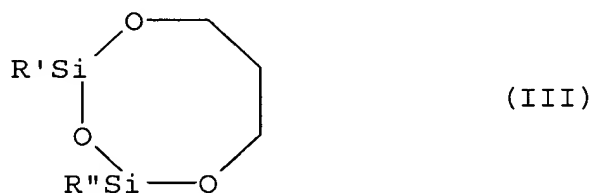
wherein

-  $R^a$  and  $R^b$  may be the same or different and are selected from the group consisting of hydrogen, alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl or are joined together to form a heterocyclic ring containing two to five carbon atoms; and

-  $R^c$  is selected from the group consisting of alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl;

-  $X_2$  is H, hydroxyl, alkylamino, alkylamido or hydroxyalkyl;

-  $X_3$  and  $X_4$  represent independently hydrogen, hydroxyl, amino, amido, azido, halo, alkyl, alkoxy, carboxy, nitrilo, nitro, trifluoro, aryl, alkaryl, thio, thioester, thioether, -OCOPh, -OC(=S)OPh or both  $X_3$  and  $X_4$  are oxygens connected to  $>C=S$  to form a 5-membered ring, or  $X_2$  and  $X_3$  form the ring of formula (III):



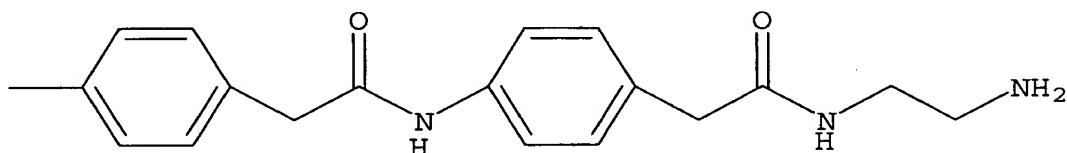
where  $R'$  and  $R''$  represent independently an alkyl group;

-  $R_2$  is selected from the group consisting of hydrogen, halo, alkylether, amino, hydrazido, alkylamino, alkoxy, thioalkoxy, pyridylthio, alkenyl; alkynyl, thio, and alkylthio; and

-  $R_3$  is a group of the formula  $-NR_4R_5$  wherein

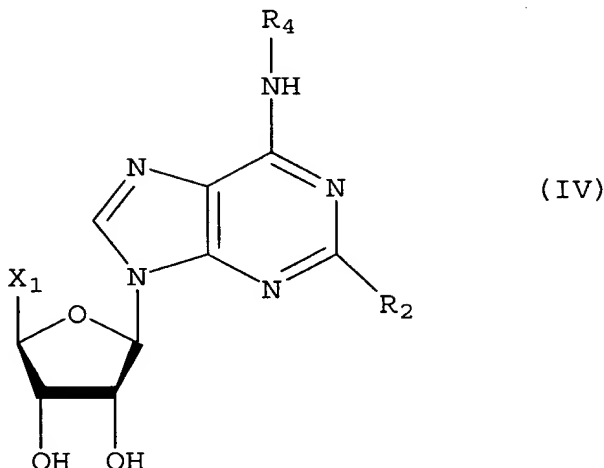
-  $R_4$  is a hydrogen atom or a group selected from alkyl, substituted alkyl or aryl-NH-C(Z)-, with Z being O, S, or NR<sup>a</sup> with R<sup>a</sup> having the above meanings; wherein when  $R_4$  is hydrogen than

-  $R_5$  is selected from the group consisting of R- and S-1-phenylethyl, benzyl, phenylethyl or anilide groups unsubstituted or substituted in one or more positions with a substituent selected from the group consisting of alkyl, amino, halo, haloalkyl, nitro, hydroxyl, acetoamido, alkoxy, and sulfonic acid or a salt thereof; benzodioxanemethyl, fururyl, L-propylalanyl-aminobenzyl,  $\beta$ -alanyl-amino-benzyl, T-BOC- $\beta$ -alanylaminobenzyl, phenylamino, carbamoyl, phenoxy or cycloalkyl; or  $R_5$  is a group of the following formula:



or when  $R_4$  is an alkyl or aryl-NH-C(Z)-, then,  $R_5$  is selected from the group consisting of heteroaryl-NR<sup>a</sup>-C(Z)-, heteroaryl-C(Z)-, alkaryl-NR<sup>a</sup>-C(Z)-, alkaryl-C(Z)-, aryl-NR-C(Z)- and aryl-C(Z)-; Z representing an oxygen, sulfur or amine; or a pharmaceutically acceptable salt of the above compound.

3 (Original). The method of Claim 2, wherein said A3RAg is a nucleoside derivative of the general formula (IV):



wherein  $X_1$ ,  $R_2$  and  $R_4$  are as defined in Claim 2.

4 (Previously Presented). The method of Claim 3, wherein A3Rag is selected from the group consisting of  $N^6$ -2-(4-aminophenyl)ethyladenosine (APNEA),  $N^6$ -(4-amino-3-iodobenzyl)adenosine-5'-(N-methyluronamide) (AB-MECA) and  $N^6$ -(2-iodobenzyl)-adenosine-5'-N-methyl-uronamide (IB-MECA) and 2-chloro- $N^6$ -(2-iodobenzyl)-adenosine-5'-N-methyluronamide (Cl-IB-MECA).

5 (Original). The method of Claim 4, wherein A3Rag is IB-MECA or Cl-IB-MECA.

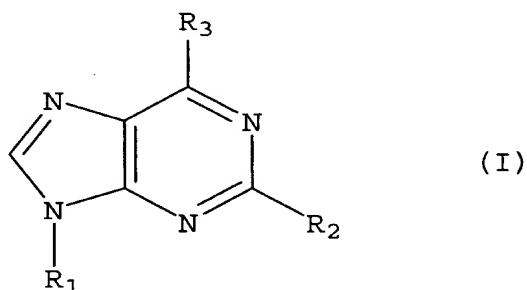
6 (Currently Amended). The method of Claim 139, wherein said A3Rag is  $N^6$ -benzyladenosine-5'-N-alkyluronamide- $N^1$ -oxide or  $N^6$ -benzyladenosine-5'-N-dialkyluronamide- $N^1$ -oxide, both optionally substituted at the 2-purine position with an alkoxy, amino, alkenyl, alkynyl or halogenoxide group.

7 (Currently Amended). The method of Claim ~~4~~39 wherein said A3RAG is administered orally to said individual.

8 (Currently Amended). The method of Claim ~~4~~39, wherein said A3RAG is injected to said individual.

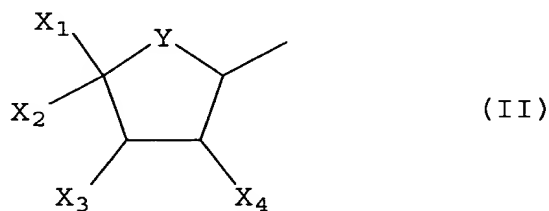
9 (Canceled)

10 (Currently Amended). The method of Claim ~~9~~40, wherein said A3RAG is a compound of the general formula (I):



wherein,

-  $R_1$  represents an alkyl, hydroxyalkyl, carboxyalkyl or cyanoalkyl or a group of the following general formula (II):



in which:

- $Y$  represents an oxygen or sulfur atom or  $CH_2$ ;
- $X_1$  represents H, alkyl,  $R^aR^bNC(=O)-$  or  $HOR^c-$ ,

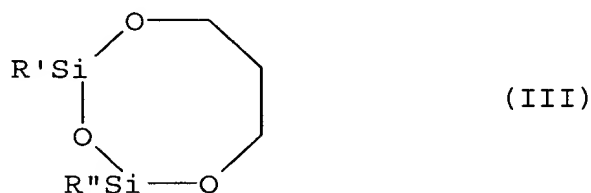
wherein

-  $R^a$  and  $R^b$  may be the same or different and are selected from the group consisting of hydrogen, alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl or are joined together to form a heterocyclic ring containing two to five carbon atoms; and

-  $R^c$  is selected from the group consisting of alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl;

-  $X_2$  is H, hydroxyl, alkylamino, alkylamido or hydroxyalkyl;

-  $X_3$  and  $X_4$  represent independently hydrogen, hydroxyl, amino, amido, azido, halo, alkyl, alkoxy, carboxy, nitrilo, nitro, trifluoro, aryl, alkaryl, thio, thioester, thioether, -OCOPh, -OC(=S)OPh or both  $X_3$  and  $X_4$  are oxygens connected to  $>C=S$  to form a 5-membered ring, or  $X_2$  and  $X_3$  form the ring of formula (III):



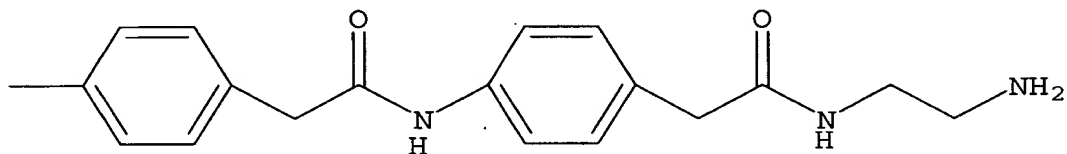
where  $R'$  and  $R''$  represent independently an alkyl group;

-  $R_2$  is selected from the group consisting of hydrogen, halo, alkylether, amino, hydrazido, alkylamino, alkoxy, thioalkoxy, pyridylthio, alkenyl; alkynyl, thio, and alkylthio; and

-  $R_3$  is a group of the formula  $-NR_4R_5$  wherein

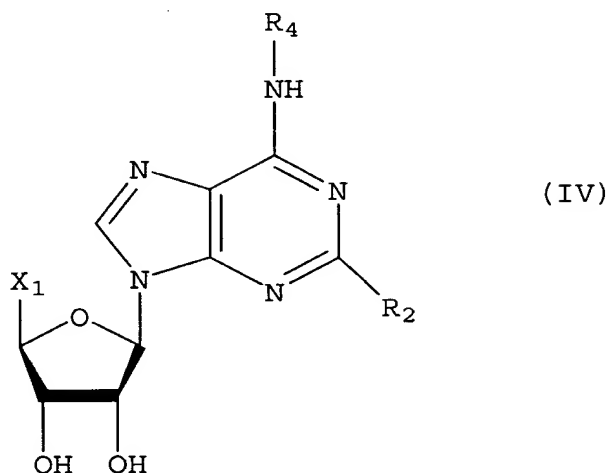
-  $R_4$  is a hydrogen atom or a group selected from alkyl, substituted alkyl or aryl-NH-C(Z)-, with Z being O, S, or NR<sup>a</sup> with R<sup>a</sup> having the above meanings; wherein when  $R_4$  is hydrogen than

-  $R_5$  is selected from the group consisting of R- and S-1-phenylethyl, benzyl, phenylethyl or anilide groups unsubstituted or substituted in one or more positions with a substituent selected from the group consisting of alkyl, amino, halo, haloalkyl, nitro, hydroxyl, acetoamido, alkoxy, and sulfonic acid or a salt thereof; benzodioxanemethyl, fururyl, L-propylalanyl-aminobenzyl,  $\beta$ -alanyl-amino-benzyl, T-BOC- $\beta$ -alanylaminobenzyl, phenylamino, carbamoyl, phenoxy or cycloalkyl; or  $R_5$  is a group of the following formula:



or when  $R_4$  is an alkyl or aryl-NH-C(Z)-, then,  $R_5$  is selected from the group consisting of heteroaryl-NR<sup>a</sup>-C(Z)-, heteroaryl-C(Z)-, alkaryl-NR<sup>a</sup>-C(Z)-, alkaryl-C(Z)-, aryl-NR-C(Z)- and aryl-C(Z)-; Z representing an oxygen, sulfur or amine; or a pharmaceutically acceptable salt of the above compound.

11 (Original). The method of Claim 10, wherein said A3RAg is a nucleoside derivative of the general formula (IV):



wherein  $X_1$ ,  $R_2$  and  $R_4$  are as defined.

12 (Previously Presented). The method of Claim 11, wherein said A3RAg is selected from the group consisting of  $N^6$ -2-(4-aminophenyl)ethyladenosine (APNEA),  $N^6$ -(4-amino-3-iodobenzyl)adenosine-5'-(N-methyluronamide) (AB-MECA) and  $N^6$ -(3-iodobenzyl)-adenosine-5'-N-methyluronamide (IB-MECA) and 2-chloro- $N^6$ -(3-iodobenzyl)-adenosine-5'-N-methyluronamide (Cl-IB-MECA).

13 (Original). The method of Claim 12, wherein said A3RAg is Cl-IB-MECA.

14 (Currently Amended). The method of Claim 940, wherein said A3RAg is  $N^6$ -benzyladenosine-5'-N-alkyluronamide- $N^1$ -oxide or  $N^6$ -benzyladenosine-5'-N-dialkyluronamide- $N^1$ -oxide, both optionally substituted at the 2-purine position with an alkoxy, amino, alkenyl, alkynyl or halogenoxide group.



15 (Currently Amended). The method of Claim 940, wherein said A3Rag is orally administered to said individual.

16 (Currently Amended). The method of Claim 940, wherein said A3Rag is injected to said individual.

17-35 (Cancelled)

36 (Currently Amended). A method in accordance with Claim 940, wherein said disease is associated with malignant cells.

37 (Currently Amended). A method in accordance with Claim 940, wherein said disease is associated with cells infected with viruses, bacteria or protozoa.

38 (Currently Amended). A method in accordance with Claim 939, wherein said individual is one affected with a treatment of a disease or disorder relates to treatment of tumor cells, a malignant and or infectious diseases, or a disease or disorder requiring immunoregulation, hematopoiesis, or neuroendocrine interactions.

39 (New). A method for treating a human individual affected with a disease or disorder that may be ameliorated through activation of natural killer (NK) cells, comprising:

- (i) determining that said disease or disorder is one that may be ameliorated through activation of NK cells, and

Appln. No. 09/832,818

Amdt. dated April 18, 2005

Reply to Office action of November 16, 2004

(ii) administering to the individual one or more adenosine A3 receptor agonists (A3RAg) in an amount effective for fully or partially activating adenosine A3 receptors on said NK cells thereby activating said NK cells.

40 (New). A method for treating a human individual affected with a disease or disorder selected from malignant and infectious diseases, the method comprising administering to the individual one or more adenosine A3 receptor agonists (A3RAg) in an amount effective for fully or partially activating adenosine A3 receptors on natural killer (NK) cells thereby activating said NK cells.